

DETECTION OF NUCLEIC ACID POLYMORPHISM

Abstract

This document describes a method of detecting DNA variation by monitoring the formation or dissociation of a complex consisting of: (a) a single strand of a DNA sequence containing the locus of a variation, (b) an oligonucleotide or DNA analogue probe specific for one allele of the variation and capable of hybridizing to the single strand (a) to form a duplex, a marker specific for the duplex structure of (a) plus (b) which forms a complex with the said duplex and reacts uniquely when interacting within the duplex, which comprises continually measuring an output signal indicative of interaction of the marker with duplex formed from the strand (a) and probe (b) and recording the conditions at which a change in reaction output signal occurs which is attributable to formation or dissociation of the complex and is thereby correlated with the strength with which the probe (b) has hybridized to the single strand (a). The method, termed Dynamic Allele Specific Hybridization (DASH), scores nucleotide differences in DNA sequences. Fluorescent markers are convenient as markers to underline variations in fluorescence resulting from denaturation or hybridization of the complex.